Severe Tracheomalacia in the ICU: Identification of Diagnostic Criteria and Risk Factor Analysis From a Case Control Study

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BACKGROUND: Severe tracheomalacia (STM) is being increasingly recognized as a cause for respiratory failure in the ICU. The diagnosis is often overlooked, as chest radiography appears normal, and the role of invasive diagnostic testing for this diagnosis is not well described in the ICU setting. The prevalence and risk factors for STM are not known, and computed tomography (CT) based diagnostic criteria for ventilated patients are not well studied. METHODS: Patients admitted between January 2008 and December 2010, with respiratory failure and who failed ventilator discontinuation or required reintubation, were screened for the presence of any tracheal collapse, utilizing prior CT of the chest. Bronchoscopically confirmed cases were compared with age and sex matched controls to identify risk factors. RESULTS: Twenty-five subjects were identified as having STM, which represented 0.7% of ICU admissions and 1.6% of subjects with respiratory failure. The mean ICU stay was significantly longer in STM (30 d, 95% CI 19.7–40 d), compared to controls (4.4 d, 95% CI 3.6–5.2 d). Obesity (odds ratio 1.26, 95% CI 1.04–1.54) and gastro-esophageal reflux (odds ratio 31, 1.7- 586) were associated with increased risk for STM. The pre-intubation P_{aCO_2} (68 mm Hg, 95% CI 57–79 mm Hg) was significantly higher in STM, compared to controls (38 mm Hg, 95% CI 35–41). The distal tracheal antero-posterior diameter (2.80 mm, 95% CI 2.15–3.46) was significantly lower in STM. A receiver operating characteristic analysis showed a distal tracheal antero-posterior diameter < 7 mm to be the optimal cutoff measurement to diagnose STM. CONCLUSION: STM was associated with prolonged ICU stay. A distal tracheal antero-posterior diameter < 7 mm on a non-intubated CT chest was suggestive of STM that required a confirmatory bronchoscopy. Gastroesophageal reflux disease and obesity were potential risk factors. *Key words: tracheomalacia; respiratory failure; ICU; intubation; tracheal collapse; bronchoscopy; reflux; obesity*. [Respir Care 2013;58(2):340–347.

Introduction

Tracheobronchomalacia (TBM) is a condition characterized by weakness of the supporting structures of tracheal and bronchial walls, resulting in expiratory collapse, leading to symptoms of airway obstruction.[1–4] Severe TBM (STM) is increasingly recognized as a condition associated with substantial respiratory morbidity.[4] Based on radiographic estimates, the prevalence of tracheal collapse in adults varies from 7.1%[5] to 10.5% in men and 17.1% in women[6] who had chest computed tomogram (CT) as a part of pulmonary emphysema workup. In contrast to radiologic estimates, bronchoscopic evaluation in a large series referred to chest clinic for chronic bronchitis has documented an overall prevalence of TBM in 5% and STM in about 13%.[7]

Patients with STM are often admitted to ICU with respiratory failure. However, the diagnosis is usually overlooked because the admitting chest radiograph is unremarkable, and therefore the respiratory failure is often

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The authors have disclosed no conflicts of interest.

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DOI: 10.4187/respcare.01866

attributed to asthma,[8] COPD exacerbation, or severe obstructive sleep apnea.[9,10] Furthermore, orotracheal intubation in patients may delay early recognition on CT imaging of the chest, as the endotracheal tube and mechanical ventilation may prevent substantial tracheal collapse. Accordingly, the true prevalence of STM in the ICU is unknown, and there are no studies exploring the possible risk factors associated with STM.

Finally, the clinical and radiographic features in patients with STM admitted to ICU for respiratory failure have not been well characterized. Given the uncertain incidence and under-recognition of STM, this study was performed to identify the prevalence in patients in the ICU with severe respiratory failure, to explore risk factors associated with STM, and to identify clinical and radiological features helpful in diagnosing this entity in the ICU.

QUICK LOOK

Current knowledge

Tracheobronchomalacia is a condition characterized by weakness of the supporting structures of tracheal and bronchial walls, resulting in expiratory collapse, leading to symptoms of airway obstruction. Severe tracheobronchomalacia is increasingly recognized as a condition associated with substantial respiratory morbidity. The true prevalence of severe tracheobronchomalacia in the ICU and its risk factors are unknown.

What this paper contributes to our knowledge

Severe tracheobronchomalacia is associated with hypercapnic respiratory failure and prolonged ICU stay. Obesity and the presence of gastroesophageal reflux disease are risk factors. An anterior posterior tracheal diameter on a pre-intubation computed tomogram measuring < 7 mm in an intubated patient suggests the possibility of severe tracheobronchomalacia.

Methods

The study was a single center prospective study conducted at a 650-bed tertiary university hospital from January 2008 to December 2010. Patients who were admitted to the ICU with respiratory failure and who experienced failed extubation after passing a spontaneous breathing trial with endotracheal tube in place were the subjects of this study. These subjects were screened for presence of distal tracheal narrowing, using a CT of the chest obtained during a previous hospitalization. If the previous pre-intubation CT finding was suggestive of tracheal collapse in a subject, this subject was scheduled for a confirmatory bronchoscopy, per the protocol described below. In all, 28 consecutive subjects were indentified to have substantial tracheal collapse as evidenced by $> 50\%$ collapse of the distal trachea on a pre-intubation CT of the chest done within 12 months prior to admission. Although 3 of these subjects had CT of the chest evidence of tracheal collapse, they did not meet the study's strict bronchoscopic criteria of complete lumen occlusion on passive exhalation, and therefore were excluded from the analysis. Furthermore, none of our subjects had a previous lung function study available for analysis. A case control methodology was adapted to identify the possible risk factors associated with STM. The study proposal and conduct of the study was approved by University of California, San Francisco–Fresno, institutional review board (approval 2008089).

Bronchoscopic Conformation of STM

When cases met the inclusion criteria, a diagnostic bronchoscopy was done using the following protocol: under conscious sedation and F_{IO_2} of 1.0, a bronchoscope (BF-P180, Olympus, Tokyo, Japan) was introduced through the cuffed endotracheal tube and advanced beyond the tip of the endotracheal tube. Following this, the cuff was deflated, then the endotracheal tube was carefully withdrawn to place the tip just below the first tracheal ring, and the cuff was re-inflated. Finally, the PEEP was reduced to zero before examination for tracheal collapse during passive exhalation. STM was diagnosed if there was complete occlusion of the distal trachea during passive exhalation. To minimize inter-observer variability, all bronchoscopic confirmation was done by a single pulmonologist (JJV), and digital images were captured and placed in patient records. At the end of the examination the PEEP was returned to the previous level to document a lack of collapse of the distal trachea on passive exhalation during mechanical ventilation.

Selection of Controls

Subjects who were age and sex matched and admitted to the medical ICU for respiratory failure during the same time period, and had an available CT of the chest prior to intubation were recruited as control subjects. For every STM subject, 2 age and sex matched controls were recruited. The primary diagnoses in the control subjects included: sepsis and respiratory failure in 12, pneumonia and respiratory failure in 10, congestive heart failure with pulmonary edema in 10, renal failure with fluid overload in 9, and COPD exacerbation in 9. Subjects with malignancy were excluded. Finally, to obtain measurements of the tracheal and bronchial tree in normal subjects, patients between the ages of 18 and 75 years who had a CT scan of the chest in the emergency department, either for dyspnea or chest pain, but did not have any clinical evidence of COPD, asthma, or obstructive sleep apnea were recruited.

Clinical variables gathered included age, sex, smoking status, body mass index, prior glucocorticoid use, history of radiation therapy to the chest or chemotherapy for malignancy, prior history of COPD, gastroesophageal reflux disease (GERD), and arterial blood gas values. Finally, the following outcome variables were also collected from study subjects: ICU stay, permanent tracheostomy status, and the need for tracheal stent.

Measurements of Tracheal and Bronchial Diameter on CT of the Chest

In consultation with a radiologist, the following measurements were obtained from a CT of the chest in all study subjects. The length of the trachea was measured as the distance between the lower aspect of the vocal cords and a point 2 mm above the tracheal bifurcation on the scout film of the CT chest. The proximal tracheal measurements (antero-posterior and horizontal diameter and area) were taken just below the vocal cords, mid-tracheal measurements were done at the level of the aortic arch, and distal tracheal measurements were obtained from a point 2 mm above the carina. The right and left main bronchus measurements were done at the origin. Finally, the chest wall horizontal and antero-posterior diameter was measured at the level of the carina.

Statistical Analysis

Continuous variables between the 2 groups were compared using the Student *t* test. Continuous variables within 3 groups of study subjects were compared using analysis of variance. Categorical variables in study subjects were compared using chi-square analysis, and odds ratios were estimated. Multivariate analyses of risk factors were done using logistic regression analysis. Receiver operating characteristic curve analysis and area under the curve were estimated for the optimal CT chest measurements for the diagnosis of STM. All analyses were done using statistics software (SPSS 18, SPSS, Chicago, Illinois). A P value of $< .05$ was considered statistically significant.

Results

Twenty-five cases were identified over a 3-year period from a single critical care unit. They represented 0.7% of total ICU admissions (25/3,576), 1.6% of all patients with respiratory failure (25/1,582), but 21.9% of patients who required reintubation due to a failed extubation attempt within 12 hours at least one time (25/114). There were 10 males and 15 females, and their mean ± SD age was 61 ± 13.9 years. The ethnicity of study subjects was white in 68%, Hispanic in 24%, and Asian in 8%. An example of the CT chest and the corresponding static bronchoscopy image finding in a subject with STM is shown in Figure 1. The baseline characteristics of STM subjects, compared to controls, showed several important differences (Table 1). On multivariate analysis of risk factors, obesity (odds ra-

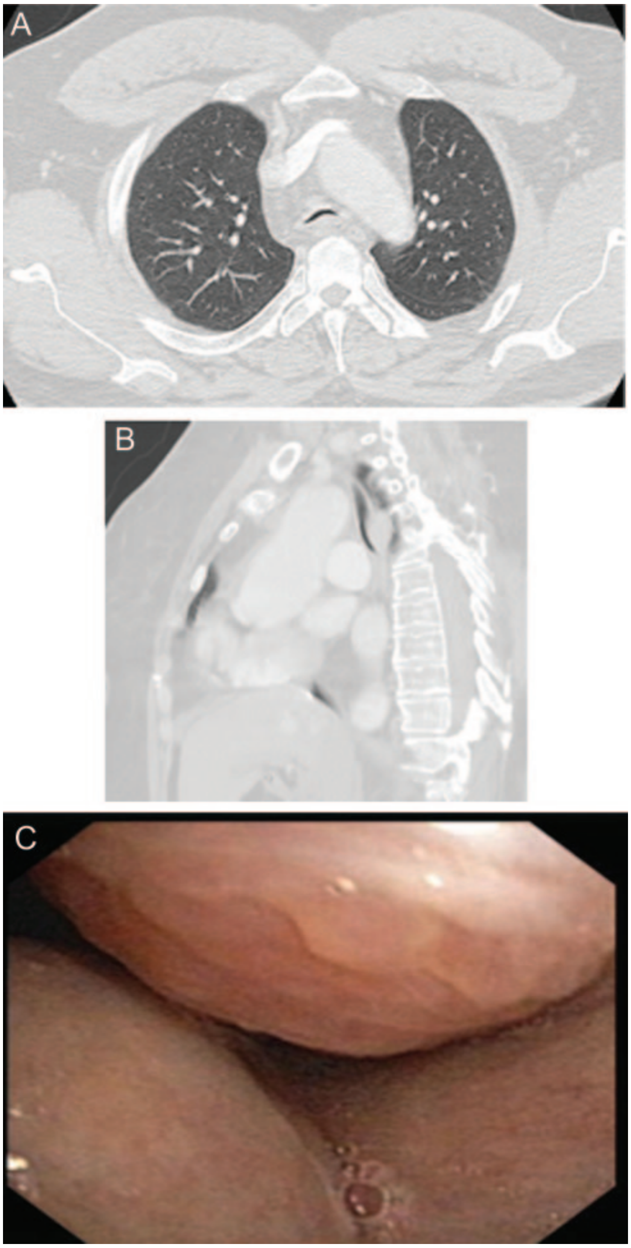

Fig. 1. A: Pre-intubation chest computed tomogram image showing substantial narrowing of the distal tracheal antero-posterior diameter (crescent sign) with normal lung parenchyma. B: Lateral view shows gradual narrowing of tracheal antero-posterior diameter from proximal to distal end. C: Bronchoscopic image taken at the end of expiration with zero PEEP, demonstrating complete collapse of the trachea.

Table 1. Subject Characteristics

	Controls (n = 50)	Cases (n = 25)	Odds Ratio	95% CI	P
Age, mean (95% CI), y	61 (57–65)	61 (55–67)	ND	ND	.85
Weight, mean (95% CI), kg	79 (73–85)	99 (86–111)	ND	ND	.007*
Height, mean (95% CI), m	1.6 (1.6–1.7)	1.6 (1.5–1.7)	ND	ND	.21
Body mass index, mean (95% CI), kg/m^2	28 (27–31)	38 (33–42)	ND	ND	.001*
ICU stay, mean (95% CI), d	4.4 (3.6–5.2)	30 (19.7–40)	ND	ND	< .001
Male/female, no.	18/32	9/16	1	0.36–2.71	> .99
Smoking, no. (%)	22 (44)	12 (48)	1.17	0.48–3.0	.80
Previous intubation, no. (%)	3 (6)	22 (88)	82	17–400	< .001†
Cough, no. (%)	4 (8)	19 (76)	36	9–144	< .001†
Dyspnea, no. (%)	41 (82)	21 (84)	1.15	0.3–4	> .99
Gastroesophageal reflux, no. (%)	6 (12)	10 (40)	4.3	1.3–14	.01†

* Significant by Student t test.
† Significant by Fisher exact test.
ND = no data because not calculated.

Table 2. Pre-intubation Arterial Blood Gas Values in Study Subjects

	n	Mean ± SD	P	95% CI
pH				
Matched controls	31	7.41 ± 0.05	.001*	7.39–7.43
Cases	24	7.32 ± 0.12		7.27–7.38
P_{aCO_2}				
Matched controls	31	38 ± 9	< .001*	35–41
Cases	24	68 ± 26		57–79
P_{aO_2}†				
Matched controls	31	99 ± 40	0.27	80–109
Cases	24	114 ± 84		78–149

* Significant by Student t test.
† P_{aO_2} measurement was done on varying F_{IO_2}.

tio 1.26, 95% CI 1.04–1.54) and GERD (odds ratio 31, 95% CI 1.7–586) were significantly associated with STM.

A comparison of arterial blood gas values in study subjects prior to intubation was performed (Table 2). Subjects with STM presented with significantly lower pH (7.32 vs 7.41) and higher P_{aCO_2}, compared to matched controls. However, P_{aCO_2} values were normal in 4 cases. The results of a comparison analysis of various tracheal measurements in cases, matched controls, and normal subjects are provided in Table 3. The mean distal tracheal antero-posterior diameter in cases (2.8 mm, 95% CI 2.15–3.46 mm) was significantly lower, compared to controls (12.9 mm, 95% CI 12.23–13.56 mm). Similarly the mean distal tracheal area in cases (69 mm^2, 95% CI 53– 85 mm^2) was significantly lower, compared to controls (233 mm^2, 95% CI 213–253 mm^2). The mean antero-posterior and horizontal diameter measurements and ratios of antero-posterior diameter to horizontal diameter are shown in Figure 2 and Table 4. Receiver operating characteristic analyses showed that a distal antero-posterior diameter of < 7 mm was significantly associated with clinically important STM (Table 5).

The mean ICU stay was significantly longer in STM cases (30 d, 95% CI 19.7–40.0 d), compared to controls (4.4 d, 95% CI 3.6–5.2 d). The 30-day mortality in our STM cases was 8% (2/25). Of the 25 cases of TBM, 6 subjects received tracheal stent placement, 17 had tracheotomy with long tracheotomy tube placement, and 2 were discharged with chronic noninvasive ventilation. Four of the 6 subjects who initially received tracheal stents were readmitted with stent migration necessitating permanent tracheotomy. Two subjects who received stent placement and 5 subjects who received tracheotomy required long-term ventilation, as the STM was diffuse, involving first and second generation bronchi.

Discussion

Although infrequent as a cause for respiratory failure in general, STM was observed in 22% of subjects who underwent reintubation. These subjects passed a spontaneous breathing trial while intubated and disconnected from the ventilator, yet developed respiratory distress soon after removal of the endotracheal tube. Furthermore, we identified GERD, chronic cough, and obesity as potential risk factors associated with STM. Finally, we identified criteria helpful for screening STM based on various tracheal measurements drawn from a pre-intubation CT of the chest. This study should serve to improve diagnosis of this rare entity among hypercapnic respiratory failure patients who fail extubation attempts.

TBM is a condition characterized by weakness of the

Table 3. Tracheal Measurements in Study Subjects

	Subject Type	n	Mean	95% CI	P
Length of trachea, mm	Normal subjects	58	114.61	109.45–119.77	.39
	Matched controls	50	111.79	106.85–116.73	
	Cases	25	118.07	109.81–126.33	
Proximal anterior-posterior tracheal diameter, mm	Normal subjects	58	16.70	15.79–17.62	.001*
	Matched controls	50	16.64	15.65–17.63	
	Cases	25	13.47	11.29–15.65	
Mid anterior-posterior tracheal diameter, mm	Normal subjects	58	15.65	14.83–16.46	< .001*
	Matched controls	50	15.80	14.91–16.69	
	Cases	25	8.39	6.30–10.49	
Distal anterior-posterior tracheal diameter, mm	Normal subjects	58	13.41	12.69–14.12	< .001*
	Matched controls	50	12.90	12.23–13.56	
	Cases	25	2.80	2.15–3.46	
Proximal horizontal tracheal diameter, mm	Normal subjects	58	14.83	13.92–15.74	.06
	Matched controls	50	14.06	13.11–15.02	
	Cases	25	12.74	10.89–14.60	
Mid horizontal tracheal diameter, mm	Normal subjects	58	15.68	15.02–16.34	< .001*
	Matched controls	50	15.90	15.23–16.58	
	Cases	25	11.89	9.97–13.80	
Distal horizontal tracheal diameter, mm	Normal subjects	58	20.16	18.75–21.56	< .001*
	Matched controls	50	19.20	17.93–20.47	
	Cases	25	11.97	9.79–14.15	
Proximal tracheal area, mm^2	Normal subjects	58	212.34	191.19–233.49	.39
	Matched controls	50	223.44	194.99–251.89	
	Cases	25	192.20	150.04–234.35	
Mid tracheal area, mm^2	Normal subjects	58	207.93	193.04–222.82	< .001*
	Matched controls	50	217.11	200.49–233.72	
	Cases	25	92.72	60.28–125.16	
Distal tracheal area, mm^2	Normal subjects	58	228.61	205.53–251.69	< .001*
	Matched controls	50	233.61	213.40–253.81	
	Cases	25	69.03	53.05–85.00	

* Significant by analysis of variance.

supporting structures of tracheal and bronchial walls, resulting in expiratory collapse, leading to symptoms of airway obstruction. Although there are several case reports, case series, and reviews in children describing the pathogenesis of TBM,[4] there is a paucity of literature regarding the pathogenesis of the acquired form of TBM in adults. Developmental anomalies, including faulty foregut division, have been proposed as a mechanism for TBM in children.[11–13] The pathological findings described in children with TBM include reduction in the number of longitudinal fibers, atrophy of the longitudinal elastic fibers of the pars membranacea, and fragmentation of tracheal cartilage.[14,15] Whether similar histopathological findings may explain the pathogenesis of acquired STM in adults remain unanswered.

The prevalence of GERD was increased in subjects with STM, compared to age and sex matched controls: a finding that has not been reported before. It is possible that repeated exposure of tracheal tissue to an acid milieu and digestive enzymes from GERD might alter the matrix protein structure, resulting in reduced tensile strength of tracheal tissue, leading to STM.[16,17] In this setting, alterations in mechanical forces induced signaling mechanisms in maintaining the plasticity and structural organization of airway smooth muscle of the trachea may be important.[18–20] Although in bivariate analysis the incidence of chronic cough was increased in subjects with STM, compared to age and sex matched controls, multivariate analysis did not show a significant association, suggesting cough as a confounding variable. As our sample size was relatively small and there was a potential for recall bias, a large prospective study is required to ascertain the association between chronic cough and GERD in STM.

Finally, subjects with STM were found to be obese, compared to matched controls. Obesity as a risk for STM has not been reported previously. However, obesity has been found to be an independent risk factor for GERD.[21–23] Therefore, the role of obesity and GERD as independent risk factors for STM and the possibility for interaction between obesity and GERD merit further investigation using a larger sample size.

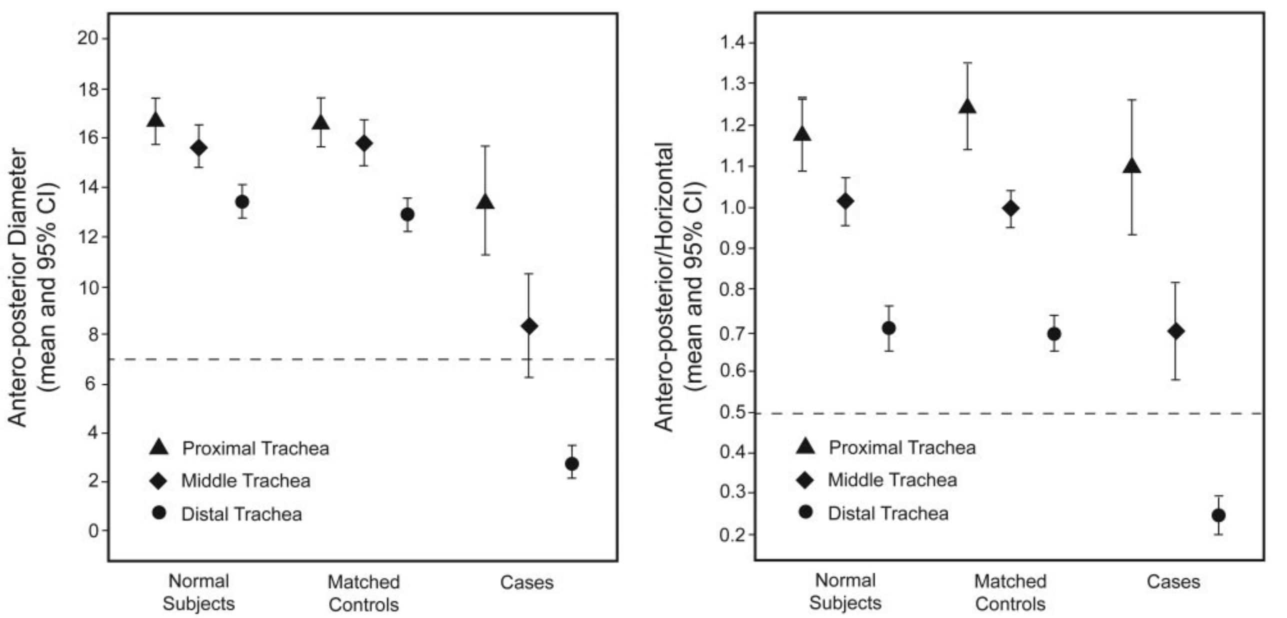

Fig. 2. The mean antero-posterior diameter and antero-posterior/horizontal ratio decreased progressively from proximal to distal trachea in all study subjects. However, the degree of reduction in antero-posterior diameter was steep in the cases, compared to the normal subjects and matched controls. The dashed lines represent the optimal cutoff values for antero-posterior diameter and antero-posterior/horizontal ratio to diagnose severe tracheomalacia.

Table 4. Anterior-Posterior/Horizontal Ratios in Study Subjects

		n	Mean	*P*	95% CI
Anterior-posterior to horizontal diameter ratio proximal trachea	Normal subjects	58	1.18	.24	1.09–1.26
	Matched controls	50	1.25		1.14–1.35
	Cases	25	1.10		0.93–1.26
Anterior-posterior to horizontal diameter ratio middle trachea	Normal subjects	58	1.02	< .001*	0.96–1.07
	Matched controls	50	1.00		0.95–1.04
	Cases	25	0.70		0.58–0.82
Anterior-posterior to horizontal diameter ratio distal trachea	Normal subjects	58	0.71	< .001*	0.65–0.76
	Matched controls	50	0.69		0.65–0.74
	Total	133	0.61		0.57–0.66

* Significant by analysis of variance.

Table 5. Area Under the Curve for Tracheal Measurements

	Area	Standard Error	*P*	95% CI
Distal anterior-posterior tracheal diameter	1.000	0	< .001	1.000–1.000
Distal tracheal area	0.998	0.003	< .001	0.992–1.000
Anterior-posterior to horizontal diameter ratio of distal trachea	0.991	0.009	< .001	0.973–1.000
Right main bronchus anterior-posterior diameter	0.998	0.002	< .001	0.994–1.000
Left main bronchus anterior-posterior diameter	0.987	0.011	< .001	0.966–1.000

Lack of recognition of STM as a cause for respiratory failure, and failure to liberate from the ventilator may result in prolonged ICU stay and recurrent ICU admissions. Although CT evidence for severe distal tracheal collapse was present in all cases, there was no reference to this abnormal finding in 95% of radiology reports. We attribute this to the lack of awareness of this entity. The results of this study will likely increase the awareness of

STM and therefore aid in earlier recognition of STM in ventilated patients with respiratory failure.

As a prior CT scan of the chest was utilized to screen subjects for tracheal collapse, it is possible that we may have missed a few subjects with STM who did not have an available prior CT chest. Also, we used complete collapse as the criteria for STM and, therefore, generalization of our results to mild to moderate tracheal collapse should be made with caution. As the study subjects were matched for age and sex, the potential role of these 2 important variables could not be analyzed in this case control study. Ethnicity has been known to affect airway measurements; the effect of this variable has not been assessed in this study. Furthermore, identification of risk factors was based on chart review; therefore, there is a potential for recall bias, as expected in any retrospective data collection.

It is possible that some of our subjects may have undiagnosed obstructive sleep apnea or COPD as an additional cause for hypercapnic respiratory failure. However, subjects tolerating a spontaneous breathing trial while intubated and disconnected from the ventilator and subsequently developing respiratory distress soon after extubation may suggest tracheal collapse as a trigger for respiratory distress. Some of the study subjects were suspected to have obstructive sleep apnea, based on hypercapnic respiratory failure. However, obstructive sleep apnea cannot completely explain the respiratory distress developing immediately following extubation in our study subjects, especially considering that obstructive sleep apnea requires sleeping patients to manifest itself, and OHS as a sole clinical issue is not a common cause for acute respiratory distress requiring intubation.[24] Finally, our study population reflects the experience from a tertiary hospital, and therefore the data on prevalence of STM need to be applied with caution in a general ICU population.

CPAP has been reported to be successful in treating STM,[25] presumably by working as a pneumatic stent and preventing tracheal collapse, and may have helped 2 of our subjects. Tracheal stent placement may be helpful in reducing ventilator dependence. However, stent migration, as happened in 4 of our subjects, can occur due to excessive laxity of tracheal supportive tissue. Therefore, tracheoplasty may be a better mode of intervention than tracheal stents in these subjects.[26,27] Artificial tracheal transplant may be a future consideration for STM.[28–30]

Conclusions

In conclusion, STM is associated with hypercapnic respiratory failure and prolonged ICU stay. An antero-posterior tracheal diameter on a pre-intubation CT chest measuring < 7 mm in an intubated patient should alert the clinician to the possibility of STM. Bronchoscopy showing complete occlusion of the distal trachea when PEEP is removed may suggest STM. Obesity and GERD appear to be risk factors for STM. For those patients who fail extubation in < 12 hours with a normal chest x-ray, a non-contrast CT chest may help identify STM as a cause.

ACKNOWLEDGMENTS

We thank Paul Mills MD, Department of Clinical Epidemiology, University of California, San Francisco–Fresno, for help with study design and data analysis, and Nischal Kumar for help with data collection.

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